REMARKS

Status of the Claims

As of this Amendment, claims 1, 3-8 and 28-33 are pending. Claim 2 is canceled, claims 3 and 28-30 are amended and new claims 31-33 are added. Support for new claims 31-33 is found in original claim 3. No new matter is added in any way.

Issues Under Priority

The Examiner asserts that SEQ ID NOS: 2, 3 and 4 are not found in Provisional Application 60/089,266 (filed June 15, 1998). For the following reasons, Applicants assert that SEQ ID NOS: 3 and 4 are entitled to the June 15, 1998 priority date.

Applicants agree that SEQ ID NOS: 2, 3 and 4 do not explicitly appear in the '266 priority application. However, the '266 application discloses a nucleotide sequence coding for the ABP-1 protein, whose amino acid sequence was subsequently reported in the Provisional Application 60/114,386 (filed December 29, 1998). The nucleotide sequence shown in Figure 9 of the '266 application consists of a 5' untranslated region (from nucleotide residue 1 to residue 518) followed by a coding region (from nucleotide residue 519 to residue 2540) and finally, a 3' untranslated region (from nucleotide 2541 to the end). While the 5' and 3' untranslated regions differ from the corresponding regions of SEQ ID NO: 1 in the present application, the encoded protein corresponds to the protein reported as SEQ ID NO: 3 in the present application (wherein residue 135 is Asn and residues 148

to 150 are Thr, Trp and Pro, respectively). In addition, the nucleotide sequence reported in Figure 10 of the '266 application corresponds to the sequence encoding the Big-3 fragment of SEQ ID NO: 4. Thus, Applicants assert that SEQ ID NOS: 3 and 4 are entitled to the June 15, 1998 priority date.

Issues Under Drawings

The Applicants will file corrected formal drawings upon allowance of the application.

Issues Under Specification

The Specification is objected to because the brief description of the figures lacks a separate brief description of Figures 1c, 2a and 2b. Applicants note that there is no Figure 1c. In regard to the Examiner's requirement for a brief description of Figures 2a and 2b, Applicants note that Figure 2 does not comprise 2a and 2b. Applicants have amended the Specification to include the following description for Figure 2: "Figure 2 illustrates activation of His3 and LacZ in the yeast two hybrid system upon binding of angiostatin binding protein". Support is found on page 12, lines 13-20. In addition, the description of the figure is self-evident.

Issues Under Claim Objections

Claims 28-30 are objected to under 37 CFR 1.75 as being in improper dependent form. The Examiner asserts that Claim 28 is

improperly multiply dependent because it depends from another multiple dependent claim (claim 3). The Examiner asserts that claim 28 does not further limit claims 1-8 by merely reciting an intended use. The Examiner further asserts that claim 28 is an improper dependent claim to the extent that it depends from claim 26 which is drawn to a different statutory class of invention (to a "use" and not to a peptide). Applicants respectfully request reconsideration and withdrawal of the objection.

Claim 3 is amended to not be a multiple dependent claim. Claims 28 and 29 are amended to be method claims which recite a positive step utilizing the peptide of the present claims. Thus, claim 28, as amended, further limits claims 1 and 3-8. Applicants have further amended claims 28-30 to not be dependent on claim 26. Support for the amendments to claims 28 and 29 is found in former claims 28 and 29 and on page 9, line 25 through page 10, line 2 of the instant Specification.

Issues Under 35 U.S.C. § 112, First Paragraph

Claims 1-8 and 28-30 are rejected under 35 U.S.C. § 112, first paragraph, because the Specification does not reasonably provide enablement commensurate with the scope of the claimed invention. Applicants respectfully request reconsideration and withdrawal of the rejection.

Claim 3 is rejected as encompassing "inoperative species." The Examiner states that the specification is only enabled for proteins of SEQ ID NOS: 2, 3 and 4 (ABP-1) and variants of ABP-1

that "are defined by its ability to bind a fragment of plasminogen...." Applicants have amended claim 1 (and thus, claim 3) to recite that the protein binds to an N-terminal fragment of plasminogen comprising kringle domains 1-4 and/or 5. Support for this amendment is found on page 2, lines 22-24, page 5, line 32, and on page 10, line 5 of the instant Specification.

Claims 7 and 8 are rejected as not being enabled for any protein comprising either 5 or 10 contiguous amino acids of SEQ ID NOS: 2, 3 or 4. Applicants assert that the specification fully describes how to screen proteins for plasminogen binding activity and one skilled in the art would therefore readily be able to identify proteins of claims 7 and 8. Screening techniques are described on page 8, lines 6-14, and on page 19, line 22 through page 21, line 29.

Claim 30 is rejected for recitation of the phrase "pharmaceutical composition". Applicants have amended claim 30 to recite "A composition comprising..."

Issues Under 35 U.S.C. § 112, Second Paragraph

Claims 1-4 and 28-30 are rejected as being indefinite. Applicants respectfully request reconsideration and withdrawal of the rejection.

The Examiner asserts that the phrase "angiogenesis-associated protein" in claim 1 is vague and indefinite. Applicants have amended claim 1 to remove this phrase.

The Examiner asserts that claim 3 is vague and indefinite for the recitation "having at least approximately 80% sequence homology, preferably approximately 90% sequence homology, more preferably approximately 95% sequence homology and most preferably approximately 98% sequence homology." Applicants have amended claim 3 by deleting the phrase "preferably approximately 90% sequence homology, more preferably approximately 95% sequence homology and most preferably approximately 98% sequence homology". This subject matter appears in new claims 31-33. Applicants have additionally deleted the phrase "at least".

The Examiner asserts that claim 28 is vague and indefinite in the recitation "for use as a medicament". This phrase has been deleted from claim 28. The Examiner asserts that the recitation "compounds" in claims 28 and 29 lack antecedent basis. The word "compounds" has been deleted from claims 28 and 29. The Examiner asserts that claims 29-30 are vague in their recitation of non-elected claim 26. Claims 29-30 have been amended to delete the recitation of claim 26. The Examiner asserts that claims 28-30 are vague in the recitation of "any one of the claims 1-8 and 26". Claims 28-30 have been amended to delete the recitation of claim 26. The Examiner additionally asserts that the recitation "a medicament" is vague in claims 28 and 29. The phrase "a medicament" has been deleted from claims 28 and 29.

Issues Under 35 U.S.C. § 101

Claims 29 is rejected as being directed to non-statutory subject matter. Applicants respectfully request reconsideration and withdrawal of the rejection. Claim 29 has been amended to be drawn to a method for manufacturing a composition.

Issues Under 35 U.S.C. § 102

Claims 1 and 2 have been rejected as being anticipated by Peterson et al. Claims 1, 2 and 28-30 have been rejected as being anticipated by U.S. Pat. No. 5,679,350. Peterson et al. is relied on for disclosing fibrin and U.S. '350 is relied on for disclosing uPA and tPA. The Examiner indicates that uPA and tPA both bind the N-terminal fragment of plasminogen, thus falling within the scope of claims 1 and 2. Applicants respectfully request reconsideration and withdrawal of the rejection.

INSTANT INVENTION

The instant invention is drawn to an isolated human protein, which has been named "ABP-1", involved in angiogenesis, which acts as a receptor of the N-terminal fragment of plasminogen.

PRIOR ART

Peterson et al. (Journal of Biological Chemistry 205(11):6104-6111, 1990) and U.S. Patent No. 5,679,350, disclose

tPA and uPA. The references teach that both proteins are components of the plasminogen activation system which are known to enzymatically convert plasminogen to plasmin by cleaving a specific peptide bond. Thus, tPA and uPA act enzymatically upon plasminogen and bind plasminogen in an enzyme active site.

DISTINCTIONS BETWEEN THE INSTANT INVENTION AND THE PRIOR ART

ABP-1 is distinct from the plasminogen-binding proteins of the prior art. ABP-1 is different from tPA and uPA as ABP-1 has no enzymatic activity on kringles 1-4 and/or 5 (angiostatin) of plasminogen. ABP-1 does not cleave any peptide bonds on plasminogen. The interaction between ABP-1 and angiostatin is of the receptor-ligand type in that it is merely a binding interaction without a subsequent enzymatic reaction. In a sense, a "ligand-receptor" type interaction might be characterized as a binding at an allosteric site. Binding of a ligand to its receptor typically modulates an enzymatic activity of the receptor but the ligand is not acted upon by the receptor. On the other hand, an enzyme-substrate interaction is characterized by binding of the substrate at an "active site" that not only binds the substrate but acts further upon it.

Thus, a substantial difference between the uPA and tPA enzymes of the prior art and the ABP-1 receptor of the present invention is that uPA and tPA bind plasminogen in an enzyme active site, whereas ABP-1 (and portions thereof) bind plasminogen in a ligand-receptor site. Claim 1 has been

amended to recite "An isolated human protein, having anti-angiogenic activity and that is a receptor for an N-terminal fragment of plasminogen …". As such, claim 1 is commensurate with the above argument. Therefore, the instant invention is not anticipated by Peterson et al. or by U.S. Pat. No. 5,679,350.

CONCLUSION

As the above-presented amendments and remarks address and overcome all of the rejections presented by the Examiner, withdrawal of the rejections and allowance of the claims are respectfully requested.

If the Examiner has any questions concerning this application, he is requested to contact the undersigned, at (703) 205-8000 in the Washington, D.C. area.

Pursuant to 37 C.F.R. §§ 1.17 and 1.136(a), the Applicant respectfully petitions for a one (1) month extension of time for filing a reply in connection with the present application and the required fee of $110.00 is attached hereto.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17; particularly, extension of time fees.

Respectfully submitted,

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